longer required under paragraph (c)(2) of this section. The sample submitted at the 90-day interval shall be from the first lot or filling, as applicable, released by manufacturer, under the requirements of § 610.1 of this chapter, after the end of the previous 90-day interval. The sample shall be identified as ''surveillance sample'' and shall include the date of manufacture.

(iii) Samples may at any time be required to be submitted to the Director, Center for Biologics Evaluation and Research, if the Director finds that continued evaluation is necessary to ensure the potency, quality, and reliability of the product.

(b) *Protocols.* For each sample submitted as required in paragraph (a)(1) of this section, the manufacturer shall send a protocol that consists of a summary of the history of manufacture of the product, including all results of each test for which test results are requested by the Director, Center for Biologics Evaluation and Research. The protocols submitted with the samples at periodic intervals as provided in paragraph (a)(2)(ii) of this section shall be identified by the manufacturer as ''surveillance test results.''

(c) *Offical release.* (1) The manufacturer shall not distribute the product until written notification of official release is received from the Director, Center for Biologics Evaluation and Research, except as provided in paragraph (c)(2) of this section. Official release is required for samples from at least five consecutive lots or fillings, as applicable, manufactured after licensure of the product.

(2) After written notification of official release is received from the Director, Center for Biologics Evaluation and Research, for at least five consecutive lots or fillings, as applicable, manufactured after licensure of the product, and after the manufacturer receives from the Director, Center for Biologics Evaluation and Research, written notification that official release is no longer required, subsequent lots or fillings may be released by the manufacturer under the requirements of § 610.1 of this chapter.

(3) The manufacturer shall not distribute lots or fillings, as applicable, of products that required sample submission under paragraph (a)(2)(iii) of this section until written notification of official release or notification that official release is no longer required is received from the Director, Center for Biologics Evaluation and Research.

[48 FR 20407, May 6, 1983, as amended at 49 FR 23834, June 8, 1984; 51 FR 15611, Apr. 25, 1986; 55 FR 11013 and 11014, Mar. 26, 1990]

Subpart B [Reserved]

Subpart C—Blood Grouping Reagent

SOURCE: 53 FR 12764, Apr. 19, 1988, unless otherwise noted.

§ 660.20 Blood Grouping Reagent.

(a) *Proper name and definition.* The proper name of this product shall be Blood Grouping Reagent and it shall consist of an antibody-containing fluid containing one or more of the blood grouping antibodies listed in § 660.28(d).

(b) *Source.* The source of this product shall be blood, plasma, serum, or protein-rich fluids, such as those derived from stable immunoglobulin-secreting cell lines maintained either in tissue cultures or in secondary hosts.

[53 FR 12764, Apr. 19, 1988, as amended at 65 FR 77499, Dec. 12, 2000]

§ 660.21 Processing.

(a) *Processing method.* (1) The processing method shall be one that has been shown to yield consistently a specific, potent final product, free of properties that would affect adversely the intended use of the product throughout its dating period. Stability testing shall be performed on an adequate number of representative samples of each group of products manufactured in the same fashion.

(2) Only that material that has been fully processed, thoroughly mixed in a single vessel, and filtered shall constitute a lot.

(3) A lot may be subdivided into sublots. If lots are to be subdivided, the manufacturer shall include this information in the biologics license application. The manufacturer shall describe the test specifications to verify that each sublot is identical to other sublots of the lot.

(4) Each lot of Blood Grouping Reagent shall be identified by a lot number. Each sublot shall be identified by that lot number to which a distinctive prefix or suffix shall be added. Final container and package labels shall bear the lot number and all distinctive prefixes and suffixes that have been applied to identify the sublot from which filling was accomplished.

(b) *Color coding of reagents.* Blood Grouping Reagents may be colored provided the added colorant does not adversely affect the safety, purity, or potency of the product and the colorant is approved by the Director, Center for Biologics Evaluation and Research (HFN–830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

(c) *Final containers and dropper assemblies.* Final containers and dropper pipettes shall be colorless and sufficiently transparent to permit observation of the contents to detect particulate matter or increased turbidity during use.

(d) *Volume of final product.* Each manufacturer shall identify the possible final container volumes in the biologics license application.

(e) *Date of manufacture.* The date of manufacture shall be the date the manufacturer begins the last entire group of potency tests.

[53 FR 12764, Apr. 19, 1988, as amended at 64 FR 56454, Oct. 20, 1999; 65 FR 77499, Dec. 12, 2000; 67 FR 9587, Mar. 4, 2002]

§ 660.22 Potency requirements with reference preparations.

(a) *Potency requirements.* Products for which reference Blood Grouping Reagents are available shall have a potency titer value at least equal to that of the reference preparation.

(b) *Reference preparations.* Reference Blood Grouping Reagents shall be obtained from the Center for Biologics Evaluation and Research (HFN–890), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892, and shall be used as described in the accompanying package insert for determining the potency of Blood Grouping Reagents.

[53 FR 12764, Apr. 19, 1988, as amended at 67 FR 9587, Mar. 4, 2002]

§ 660.25 Potency tests without reference preparations.

Products for which Reference Blood Grouping Reagents are not available shall be tested for potency by a method approved by the Director, Center for Biologics Evaluation and Research (HFN–830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

(a) *Potency requirements.* Blood Grouping Reagents recommended for the test tube methods, including the indirect antiglobulin tests, shall have the following potency titer values, unless other values are approved by the Director, Center for Biologics Evaluation and Research (HFN–830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

(1) For Anti-K, Anti-$\bar{k}$, Anti-Jk^a, Anti-Fy^a, Anti-C^w, at least 1+ reaction with a 1:8 dilution of the reagent.

(2) For Anti-S, Anti-$\bar{s}$, Anti-P_1, Anti-M, Anti-I, Anti-e (saline), Anti-$\bar{c}$ (saline), and Anti-A_1, at least 1+ reaction with a 1:4 dilution of the reagent.

(3) For Anti-U, Anti-Kp^a, Anti-Kp^b, Anti-Js^a, Anti-Js^b, Anti-Fy^b, Anti-N, Anti-Le^a, Anti-Le^b, Anti-Lu^a, Anti-Lu^b, Anti-Di^a, Anti-M^g, Anti-Jk^b, Anti-Co^b, Anti-Wr^a, and Anti-Xg^a, at least 2+ reaction with undiluted reagent.

(b) *Products recommended for slide tests or microplate techniques.* Blood Grouping Reagent recommended for slide test methods or microplate techniques shall produce clearly positive macroscopic results when both undiluted reagent and reagent diluted with an equal volume of diluent are tested by all methods recommended in the manufacturer's package insert using red blood cells showing heterozygous or diminished expression of the corresponding antigen. The dilution shall be made with an equal volume of compatible serum or approved diluent.

(c) *Products recomended for use in an automated system.* The manufacturer of Blood Grouping Reagent that is recommended for use in an automated system shall demonstrate that its product when used both undiluted and diluted with an equal volume of diluent satisfactorily performs when tested with